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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/743,825	01/15/2002	Rodrigo F. Chaqui	66043	8611

22242 7590 05/05/2004

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EXAMINER	
DAVIS, MINH TAM B	

ART UNIT	PAPER NUMBER
1642	13

DATE MAILED: 05/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/743,825	CHAQUI ET AL.	
	Examiner	Art Unit	
	MINH-TAM DAVIS	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,3,5-8 and 10-19* is/are pending in the application.

4a) Of the above claim(s) *6-8 and 13-16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,3,5,10-12 and 17-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *01/08/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election with traverse of group I, claims 1-5, 9-12, SEQ ID NO:1 and fragments thereof, comprising SEQ ID NO:7, 8 and 10, in Paper of 02/03/04 is acknowledged and entered. Applicant cancels claims 1, 4, 9 and adds new claims 17-19, which are related to claims 1-5, 9-12 and are not new matter.

Claims 2-3, 5-8, 10-19 are pending in the instant application and Claims 6-8, 13-16 have been withdrawn from further consideration as being drawn to non-elected invention.

Group I, Claims 2-3, 5, 10-12, 17-19, SEQ ID NO:1, 7, 8 and 10 are currently under prosecution, since new claims 17-19 have been joined with group I.

The traversal is on the following ground(s):

Group VII should be rejoined with Group I, because the restriction is within individual claims, based on whether the claim is directed to the detection of cancer cells or precancerous cells, and because a more meaningful examination of the present invention would be achieved if all such claims were examined in a single invention. Applicant submits that a more preferable procedure would be to request an election of species between cancer cells and precancerous cells.

Applicant's arguments have been considered but are found not to be persuasive for the following reasons: The methods of group VII is an additional method, using SEQ ID NO:1.

A national stage application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept. When claims to

different categories are present in the application, the claims will be considered to have unity of invention if the claims are drawn only to one of the following combinations of categories: (1) A product and a process specially adapted for the manufacture of said product; or (2) A product and a process of use of said product; or (3) A product, a process specially adapted for the manufacture of the said product, and a use of the said product; or (4) A process and an apparatus or means specifically designed for carrying out the said process; or (5) A product, a process specially adapted for the manufacture of the said product, and an apparatus or means specifically designed for carrying out the said process. If multiple products, processes of manufacture or uses are claimed, the first invention of the category first mentioned in the claims of the application will be considered as the main invention in the claims, see PCT article 17(3) (a) and 1.476 (c), 37 C.F.R. 1.475(b) and (d). Group I will be the main invention. After that, all other products and methods will be broken out as separate groups (see 37 CFR 1.475(d).).

The requirement is still deemed proper and is therefore made FINAL.

REJECTION UNDER 35 USC 112, SECOND PARAGRAPH

Claims 10-12, 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 10-12, 19 are indefinite for the use of the language "abnormally high" in claim 19. The term "abnormally high" in claim 19 is a relative term which renders the claim indefinite. The term "abnormally high" is not defined by the claim, the

specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, WRITTEN DESCRIPTION

The instant specification does not contain a written description of the invention in such full, clear, concise, and exact terms or in sufficient detail that one skilled in the art can reasonably conclude that applicant had possession of the claimed invention at the time of filing.

Claims 2-3, 5, 10-12, 17-19 are rejected under 35 USC 112, first paragraph, as lacking an adequate written description in the specification.

Claims 2-3, 5, 10-12, 17-19 are drawn to:

1) A purified nucleic acid molecule that is "complementary" to SEQ ID NO:1 (claim 17). Said nucleic acid is an RNA or a cDNA (claims 2-3),

2) A purified nucleic acid molecule that "comprises" a fragment of SEQ ID NO:1, wherein said fragment "hybridizes specifically" with SEQ ID NO:1, or a complement thereof (claim 18). Said nucleic acid "comprises" SEQ ID NO:7, 8 or 10 (claim 5), and

3) A method for detecting prostate cancer, comprising determining, in a sample of tissue or fluid of a subject, the content of a nucleic acid molecule that "comprises" a fragment of SEQ ID NO:1, wherein said fragment "hybridizes specifically" with SEQ ID NO:1, or a "complement" of SEQ ID NO:1 or a fragment thereof, wherein an abnormally

high content of said nucleic acid is indicative of the presence of prostate cancer (claims 10-12, 19).

It is noted that SEQ ID NO:7, 8 or 10 are primers, and thus are only small fragments of SEQ ID NO:1 (p.16, lines 15-16, and p. 18, lines 5-6). It is also noted that a fragment of SEQ ID NO:1 as claimed in claims 18, 19 encompasses a sequence of any size, including just a few nucleotides.

In addition, it is noted that a complement of a sequence could be partial or full complement, wherein a partial complement could share with said sequence only a few complementary nucleotides.

Moreover, it is noted that "hybridize specifically" encompass hybridizing from very low hybridization stringency to very high hybridization stringency, since there is no definition of "hybridize specifically" in the specification, and since "specifically" could be reasonably interpreted as from very low to very high specificity. It is further noted that under low hybridization conditions, unrelated sequences would hybridize to SEQ ID NO:1.

A nucleic acid molecule "comprising" a fragment of SEQ ID NO:1 or SEQ ID NO:7, 8 or 10 encompass any nucleic acid containing a fragment of SEQ ID NO:1, or containing SEQ ID NO:7, 8 or 10, and not limited to just the full length sequence, SEQ ID NO:1. The claimed nucleic acid could have any sequences attached to a fragment of SEQ ID NO:1, or to SEQ ID NO:7, 8 or 10. Said nucleic acid molecule comprising a fragment of SEQ ID NO:1 would "specifically " hybridize to SEQ ID NO:1, even under high stringency hybridization conditions, via the shared fragment. Thus there is no

limitation as to the nature of the molecules attached to a fragment of SEQ ID NO:1, or to SEQ ID NO:7, 8 or 10.

The present claim encompasses full-length genes and cDNAs that are not further described. There is substantial variability among the species of DNAs encompassed within the scope of the claims because a fragment of SEQ ID NO:1, or SEQ ID NO:7, 8 or 10 is only a fragment of any full-length gene or cDNA species. "A cDNA comprising a fragment of SEQ ID NO:1, or SEQ ID NO:7, 8 or 10" encompasses a variety of subgenera with widely varying attributes .For example,a cDNA 's principle attribute would include its coding region.A partial cDNA that did not include a disclosure of any open reading frame (ORF)of which it would be a part,would not be representative of the genus of cDNAs because no information regarding the coding capacity of any cDNA molecule would be disclosed.

Although drawn to DNA arts, the findings in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-Probe Inc. are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that [a] written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula, [or] chemical name, of the claimed subject matter sufficient to distinguish it from other materials. Id. At 1567, 43 USPQ2d at 1405. The court also stated that

> a generic statement such as "vertebrate insulin cDNA or mammalian insulin cDNA" without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.

Id. At 1568, 43 USPQ2d at 1406. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id.

Finally, the court addressed the manner by which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus. Id.

The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted

the standard that "the written description requirement can be met by "show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ....i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The inventions at issue in Lilly and Enzo were DNA constructs per se, the holdings of those cases are also applicable to claims such as those at issue here. A disclosure that does not adequately describe a product itself logically cannot adequately describe a method of using that product.

Thus, the instant specification may provide an adequate written description of a nucleic acid molecule that "comprises" a fragment of SEQ ID NO:1, or SEQ ID NO:7, 8 or 10, or a complement thereof, per Lilly by structurally describing a representative number of a nucleic acid molecule that "comprises" a fragment of SEQ ID NO:1, or SEQ ID NO:7, 8 or 10, or a complement thereof, or by describing structural features common to the members of the genus, which features constitute a substantial portion of the genus. Alternatively, per Enzo, the specification can show that the claimed invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.

In this case, the specification does not describe a nucleic acid molecule that "comprises" a fragment of SEQ ID NO:1, or SEQ ID NO:7, 8 or 10, or a complement thereof in a manner that satisfies either the Lilly or Enzo standards. The specification does not provide the complete structure of any nucleic acid molecule that "comprises" a fragment of SEQ ID NO:1, or SEQ ID NO:7, 8 or 10, or a complement thereof, other than SEQ ID NO:1, and its primers consisting of SEQ ID NO:7, 8 or 10, nor does the specification provide any partial structure of such nucleic acid molecule that "comprises" a fragment of SEQ ID NO:1, or SEQ ID NO:7, 8 or 10, or a complement thereof, nor any physical or chemical characteristics of a nucleic acid molecule that "comprises" a fragment of SEQ ID NO:1, or SEQ ID NO:7, 8 or 10, or a complement thereof, other than SEQ ID NO:1, and its primers consisting of SEQ ID NO:7, 8 or 10, nor any functional characteristics coupled with a known or disclosed correlation between structure and function. Although the specification discloses a single nucleic acid molecule, SEQ ID NO:1, and its primers consisting of SEQ ID NO:7, 8 or 10, this does not provide a description of a nucleic acid molecule that "comprises" a fragment of SEQ ID NO:1, or SEQ ID NO:7, 8 or 10, or a complement thereof that would satisfy the standard set out in Enzo.

The specification also fails to describe a nucleic acid molecule that "comprises" a fragment of SEQ ID NO:1, or SEQ ID NO:7, 8 or 10, or a complement thereof by the test set out in Lilly. The specification describes only a single nucleic acid molecule, SEQ ID NO:1, and its primers consisting of SEQ ID NO:7, 8 or 10. Therefore, it necessarily fails to describe a "representative number of such species. In addition, the

specification also does not describe structural features common to the members of the genus, which features constitute a substantial portion of the genus."

Thus, the specification does not provide an adequate written description of nucleic acid molecule, SEQ ID NO:1, and its primers consisting of SEQ ID NO:7, 8 or 10, that is required to practice the claimed invention. Further, since the specification fails to adequately describe the product that is detected by the claimed method, it also fails to adequately describe the claimed method.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, SCOPE

Claims 2-3, 5, 10-12, 17-19 are rejected under 35 U.S.C. 112, first paragraph

A. Claims 2-3, 5, 10-12, 17-19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for SEQ ID NO:1, or a nucleic acid molecule consisting of a sequence consisting of SEQ ID NO:7, 8 or 10, **does not reasonably provide enablement for a nucleic acid molecule that "comprises" a fragment of SEQ ID NO:1, or SEQ ID NO:7, 8 or 10, or a complement thereof, and a method for detecting prostate cancer by detecting the level of said nucleic acid molecule.** The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 2-3, 5, 10-12, 17-19 are drawn to:

1) A purified nucleic acid molecule that is "complementary" to SEQ ID NO:1 (claim 17). Said nucleic acid is an RNA or a cDNA (claims 2-3),

2) A purified nucleic acid molecule that "comprises" a fragment of SEQ ID NO:1, wherein said fragment "hybridizes specifically" with SEQ ID NO:1, or a complement thereof (claim 18). Said nucleic acid "comprises" SEQ ID NO:7, 8 or 10 (claim 5), and

3) A method for detecting prostate cancer, comprising determining, in a sample of tissue or fluid of a subject, the content of a nucleic acid molecule that "comprises" a fragment of SEQ ID NO:1, wherein said fragment "hybridizes specifically" with SEQ ID NO:1, or a "complement" of SEQ ID NO:1 or a fragment thereof, wherein an abnormally high content of said nucleic acid is indicative of the presence of prostate cancer (claims 10-12, 19).

It is noted that SEQ ID NO:7, 8 or 10 are primers, and thus are only small fragments of SEQ ID NO:1 (p.16, lines 15-16, and p. 18, lines 5-6). It is also noted that a fragment of SEQ ID NO:1, as claimed in claims 18-19, encompasses a sequence of any size, including just a few nucleotides.

It is further noted that a nucleic acid molecule "comprising" a fragment of SEQ ID NO:1 or SEQ ID NO:7, 8 or 10 encompass any nucleic acid containing a fragment of SEQ ID NO:1, or containing SEQ ID NO:7, 8 or 10, and not limited to just the full length sequence, SEQ ID NO:1. The claimed nucleic acid could have any sequences attached to a fragment of SEQ ID NO:1, or to SEQ ID NO:7, 8 or 10. One would expect that said nucleic acid molecule comprising a fragment of SEQ ID NO:1 would "specifically " hybridize to SEQ ID NO:1, even under high stringency hybridization conditions, via the shared fragment. Thus there is no limitation as to the nature of the molecules attached to a fragment of SEQ ID NO:1, or to SEQ ID NO:7, 8 or 10.

In addition, it is noted that a complement of a sequence could be partial or full complement, wherein a partial complement could share with said sequence only a few complementary nucleotides.

i) Applicants have not shown how to make and use the claimed numerous sequences comprising a fragment of SEQ ID NO:1, or comprising SEQ ID NO:7, 8 or 10. For example, Applicant has not taught what the structure is for the sequences attached to a fragment SEQ ID NO:18, or to SEQ ID NO:7, 8 or 10, or what the coding regions are for these sequences, or what proteins are encoded by these sequences. Further, one could not predict what the function of the claimed nucleic acids is, and whether the claimed sequences would encode a protein having the function of the full length sequence, SEQ ID NO:1, in view of teaching in the art that protein chemistry is unpredictable, and that even a single amino acid substitution or what appear to be an inconsequential chemical modification will often dramatically affect the biological activity and characteristics of a protein. The following teaching of the art, although drawn to proteins, would apply as well the claimed polynucleotides, because polynucleotide sequences encode proteins. It is well known in the art that protein chemistry is probably one of the most unpredictable areas of biotechnology. For example, Bowie et al (Science, 1990, 257 : 1306-1310) teach that an amino acid sequence encodes a message that determine the shape and function of a protein and that it is the ability of these proteins to fold into unique three-dimensional structures that allows them to function and carry out the instruction of the genome and further teaches that the problem of predicting protein structure from sequence data and in turn utilizing predicted

structural determinations to ascertain functional aspects of the protein is extremely complex (col.1, p.1306). Bowie et al further teach that while it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitution can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three dimensional structure/function relationship and these regions can tolerate only conservative substitutions or no substitutions (col.2, p.1306). The sensitivity of proteins to alterations of even a single amino acid in a sequence are exemplified by Burgess et al, (Journal of Cell Biology, 1990, 11: 2129-2138), who teach that replacement of a single lysine residue at position 118 of acidic fibroblast growth factor by glutamic acid led to the substantial loss of heparin binding, receptor binding and biological activity of the protein. In transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen (Lazar et al. Molecular and Cell Biology, 1988, 8: 1247-1252). Similarly, it has been shown that aglycosylation of antibodies reduces the resistance of the antibodies to proteolytic degradation, while CH2 deletions increase the binding affinity of the antibodies (see Tao. et al. The Journal of Immunology, 1989, 143(8): 2595-2601, and Gillies et al. Human Antibodies and Hybridomas, 1990, 1(1): 47-54). These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification will often dramatically affect the biological activity and characteristic of a protein.

The specification does not disclose how to make the claimed nucleic acid molecules, such that they would function or have the properties as claimed, or how to use said nucleic acid molecules if they did not have the function or properties claimed.

Further, the claimed method of detecting prostate cancer would be non-specific, because the claimed method would detect unrelated sequences, that comprise a fragment of SEQ ID NO:1, or comprise SEQ ID NO:7, 8 or 10, and one cannot predict whether an overexpression of the detected sequences could be found in prostate cancer.

In view of the above, it would be undue experimentation for one of skill in the art to practice the claimed invention.

ii) Moreover, it is noted that "hybridize specifically" encompass hybridizing from very low hybridization stringency to very high hybridization stringency, since there is no definition of "hybridize specifically" in the specification, and since "specifically" could be reasonably interpreted as from very low to very high specificity.

The claims encompass polynucleotides comprising non-disclosed nucleic acid sequences attached to SEQ ID NO:1. As conventionally understood in the art and as taught by US Patent No. 5,912,143, hybridization is used to refer to any process by which a strand of nucleic acid binds with a complementary strand through base pairing (col 5, lines 3-5) and further teaches that numerous equivalent conditions may be employed to comprise either low or high stringency conditions and hybridization solutions my be varied to generate conditions of either low or high stringency (col 5, lines 57-67). The "specifically hybridizes" as claimed read on both hybridizing at high

and low stringency conditions. It is well known that the lower the stringency condition the more dissimilar the hybridizing molecule will be from the molecule to which it hybridizes. For example, Sambrook et al, eds, 1989, 2nd ed, Molecular Cloning, a laboratory manual, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, p. 11.52, teach that the temperature of hybridization, (which is related to the degree of stringency) should be high enough to suppress hybridization of the probe to incorrect sequences. Sambrook et al further teach that if the probe hybridizes indiscriminately, repeat the hybridization at a higher temperature or wash under conditions of higher stringency (p. 11.52, last two lines).

When given the broadest reasonable interpretation, the claims are clearly intended to encompass a variety of species including full-length cDNAs, genes and protein coding regions. Clearly, it would be expected that a substantial number of the hybridizing molecules encompassed by the claims **would not** share either structural or functional properties with SEQ ID NO:1.

Further, the claimed method of detecting prostate cancer would be non-specific, because the claimed method would detect unrelated sequences, that comprise a fragment of SEQ ID NO:1, or comprise SEQ ID NO:7, 8 or 10, and one cannot predict whether an overexpression of the detected sequences could be found in prostate cancer.

In view of the above unpredictability, one of skill in the art would be forced into undue experimentation in order to use the claimed invention as broadly as claimed.

B. Claims 10, 12, 19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for detecting prostate cancer by detecting the level of SEQ ID NO:1 in prostate tissue, **does not reasonably provide enablement for a method for detecting prostate cancer by detecting the level of SEQ ID NO:1 in "any tissue" or "any fluid" or "any bodily fluid".** The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 10, 12, 19 are drawn to a method for detecting prostate cancer, comprising determining, in a sample of tissue or fluid or bodily fluid of a subject, the content of a nucleic acid molecule that comprises SEQ ID NO:1, or a fragment of SEQ ID NO:1, wherein said fragment hybridizes specifically with SEQ ID NO:1, or a complement of SEQ ID NO:1 or of a fragment thereof, wherein an abnormally high content of said nucleic acid is indicative of the presence of prostate cancer.

Claims 10, 12, 19 encompass a method for detecting prostate cancer, comprising determining, in a sample of "any tissue or any fluid or any bodily fluid" of a subject, the content of a nucleic acid molecule that comprises SEQ ID NO:1, or a fragment of SEQ ID NO:1, wherein said fragment hybridizes specifically with SEQ ID NO:1, or a complement of SEQ ID NO:1 or of a fragment thereof, wherein an abnormally high content of said nucleic acid is indicative of the presence of prostate cancer.

In other words, claims 10, 12, 19 encompass a method for detecting prostate cancer, comprising determining, in a sample of "any tissue or any luid or any bodily

fluid" of a subject, to which prostate cancer has metastasized, the overexpression of SEQ ID NO:1.

The specification discloses that using SEQ ID NOs:7 and 8, which are primers specific for SEQ ID NO:1 (ROO504 or PB39) (p.9), overexpression of SEQ ID NO:1 is found in prostate cancer epithelium tissue samples as compared to normal control prostate tissue (Example 3 on pages 16-17, and table 1 on page 20).

One cannot extrapolate the teaching in the specification to the scope of the claims. It is unpredictable that metastasized prostate cells still express the claimed sequences, because expression of a sequence could be lost during the progression toward metastasis. For example, Kibel, AS et al, 2000, J urol, 164(1): 192-6 teach that gene expression in the chromosomal region 12p12-13 is different in primary and metastatic prostate cancer cells, and that inactivation in the chromosome region 12p12-13 occurs prior to metastasis. Zhau, HE, 1994, J Cell Biochem, Suppl 19: 208-216, teach expression of various biomarkers associated with prostate cancer progression. Zhau et al teach that in prostate cancer, PC-3N35 subclones which are cloned from primary and metastatic sites (lymph node, kidney and bone), show difference in the levels of protein expression of various markers, such as c-erbB, vimentin, ICAM-1, cytokeratin, collagen IV between the parental PC-3N35 clone and its metastatic subclones (p.209 and table 1) and that the subline derived from the metastatic site lymph node has a 12p:17q translocation, whereas the bone-derived subline contains an isochromosome 7q (p.211, first column, first paragraph). Cheung S T et al, 2002, Cancer Research, 62(16): 4711-21, teach that from 63 metastatic clones, 39 known

genes and 24 express sequence tags are down-regulated, whereas in other 27 metastatic clones 14 known genes and 13 express sequence tags are up-regulated. Ren, C et al, 1998, Cancer Res, 58(6): 1285-90, teach a loss of expression of lysyl oxidase mRNA during progression to metastasis. Gingrich, JR et al, 1996, Cancer res, 56(18): 4096-4102 teach a loss of normal E-cadherin expression as primary tumors become less differentiated and metastasize.

Thus in view of the above, one would not have expected that the claimed sequences are useful for diagnostic information about the presence in a subject of an invasive prostate tumor.

In view of the above unpredictability, one of skill in the art would be forced into undue experimentation in order to use the claimed invention as broadly as claimed.

REJECTION UNDER 35 USC 102(a or b)

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1. Claims 17-18 are rejected under 35 U.S.C. 102(b) as being anticipated by Boehringer Mannheim Biochemicals, 1994 Catalog, p. 93.

The claims 17-18 are drawn to:

1) A purified nucleic acid molecule that is "complementary" to SEQ ID NO:1 (claim 17).

2) A complement of a purified nucleic acid molecule that "comprises" a fragment of SEQ ID NO:1, wherein said fragment "hybridizes specifically" with SEQ ID NO:1 thereof (claim 18).

It is noted that a complement of a sequence could be partial or full complement, wherein a partial complement could share with said sequence only a few complementary nucleotides.

The Boehringer Mannheim teaches a kit comprising random primers that encompass all possible 6-nucleotide sequences (see page 93, Catalog No. 1034 731/1006 924). All of the limitations of the claims are met.

2. Claims 2-3, 17-18 are rejected under 35 U.S.C. 102(a) as being anticipated by WO98/21328-A2.

The claims 2-3, 17-18 are drawn to:

1) A purified nucleic acid molecule that is "complementary" to SEQ ID NO:1 (claim 17). Said nucleic acid is an RNA or a cDNA (claims 2-3),

2) A complement of a purified nucleic acid molecule that "comprises" a fragment of SEQ ID NO:1, wherein said fragment "hybridizes specifically" with SEQ ID NO:1 thereof (claim 18).

It is noted that a complement of a sequence could be partial or full complement, wherein a partial complement could share with said sequence only a few complementary nucleotides.

WO98/21328-A2 teaches a sequence which is 99.5% similar to SEQ ID NO:1, from nucleotide 64 to nucleotide 2317, as shown in MPSRCH sequence similarity search (MPSRCH sequence search report, 2004, us-09-743-825-1.rng, pages 4-6).

All of the limitations of the claims are met.

3. Claims 2-3, 5, 17-18 are rejected under 35 U.S.C. 102(b) as being anticipated by Hudson, T, Genbank Sequence Database (Accession G22380), National Center for Biotechnology Information, National Library of Medicine, Bethesda, Maryland, publicly available on May 31, 1996 .

Claims 2-3, 5, 17-18 are drawn to:

1) A purified nucleic acid molecule that is "complementary" to SEQ ID NO:1 (claim 17). Said nucleic acid is an RNA or a cDNA (claims 2-3),

2) A purified nucleic acid molecule that "comprises" a fragment of SEQ ID NO:1, wherein said fragment "hybridizes specifically" with SEQ ID NO:1, or a complement thereof (claim 18). Said nucleic acid "comprises" SEQ ID NO:7, 8 or 10 (claim 5).

It is noted that a complement of a sequence could be partial or full complement, wherein a partial complement could share with said sequence only a few complementary nucleotides.

Moreover, it is noted that "hybridize specifically" encompass hybridizing from very low hybridization stringency to very high hybridization stringency, since there is no

definition of "hybridize specifically" in the specification, and since "specifically" could be reasonably interpreted as from very low to very high specificity. It is further noted that under low hybridization conditions, unrelated sequences would hybridize to SEQ ID NO:1.

It is also noted that a fragment of SEQ ID NO:1, as claimed in claim 18, encompasses a sequence of any size, including just a few nucleotides.

It is further noted that a nucleic acid molecule "comprising" a fragment of SEQ ID NO:1 or SEQ ID NO:7, 8 or 10 encompasses any nucleic acid containing a fragment of SEQ ID NO:1, or containing SEQ ID NO:7, 8 or 10, and not limited to just the full length sequence, SEQ ID NO:1. The claimed nucleic acid could have any sequences attached to a fragment of SEQ ID NO:1, or to SEQ ID NO:7, 8 or 10. One would expect that said nucleic acid molecule comprising a fragment of SEQ ID NO:1 would "specifically " hybridize to SEQ ID NO:1, even under high stringency hybridization conditions, via the shared fragment.

Hudson, T teaches a sequence which is 100% similar to the full length SEQ ID NO:7, from nucleotide 1 to nucleotide 22, and which is 100% similar to the full length SEQ ID NO:10, from nucleotide 1 to nucleotide 20, as shown by sequence similarity search (MPSRCH search report, 2004, us-09-743-825-7.rge, p. 1-2, and us-09-743-825-10.rge, p.1-2).

Thus the sequence taught by the art seems to be the same as the claimed sequence.

Although the reference does not specifically teach that the polynucleotide sequence hybridizes specifically to SEQ ID NO:1, however, the claimed nucleic acid molecule appears to be the same as the prior art polynucleotide sequence. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable diffrences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 571-272-0830. The examiner can normally be reached on 9:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, YVONNE EYLER can be reached on 571-272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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MINH TAM DAVIS

SUSAN UNGAR, PH.D
PRIMARY EXAMINER